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## **Selenium-Containing heterocycles from isoselenocyanates: synthesis of 5-Amino-2,4-dihydro-3H-1,2,4-triazole-3-selones**

Sommen, G L ; Linden, Anthony ; Heimgartner, H

**Abstract:** The reaction of S-methylisothiosemicarbazide hydroiodide (= S-methyl hydrazinecarboximidothioate hydroiodide; 1), prepared from thiosemicarbazide by treatment with MeI in EtOH, and aryl isoselenocyanates 5 in CH<sub>2</sub>Cl<sub>2</sub> affords 3H-1,2,4-triazole-3-selone derivatives 7 in good yield (Scheme 2, Table 1). During attempted crystallization, these products undergo an oxidative dimerization to give the corresponding bis(4H-1,2,4-triazol-3-yl) diselenides 11 (Scheme 3). The structure of 11a was established by X-ray crystallography.

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**Selenium-Containing Heterocycles From Isoselenocyanates:  
Synthesis of 5-Amino-3,4-dihydro-2*H*-1,2,4-triazole-3-selones**

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The reaction of the hydroiodide of *S*-methyl isothiosemicarbazide (**1**), prepared from thiosemicarbazide by treatment with MeI in EtOH, and aryl isoselenocyanates **5** in CH<sub>2</sub>Cl<sub>2</sub> affords 1,2,4-triazole-3-selone derivatives **7** in good yield. During attempted crystallization, these products undergo an oxidative dimerization to give the corresponding bis(4*H*-1,2,4-triazol-3-yl)diselenides **11**. The structure of **11a** has been established by X-ray crystallography.

**1. Introduction.** – The biochemistry and pharmacology of selenium is of current interest, particularly with regard to public health. Selenium has long been recognized as a dietary antioxidant and is now known to be an essential component to the active sites of several enzymes, including glutathione peroxidase [1] and thioredoxine reductase, which catalyze reactions essential for the protection of cellular components against oxidative and free radical damage [2]. A too low concentration of selenium in the plasma has been identified as a risk factor for several diseases, including cancer [3], cardiovascular disease [4], osteoarthritis or AIDS [5]. Therefore, consumption of Se-rich plants or yeast-based nutritional supplements is reported to reduce the risk of cancer. It has also been suggested that plants are able to convert inorganic Se in the soil or growth medium into organoselenium compounds, such as selenoamino acids [6], by following a route similar to the sulfur assimilatory pathway [7].

In recent years, the interest in organoselenium chemistry increased remarkably. There is no doubt that Se-containing organic molecules have played and continue to play an important role in biology and medicine, and a large number of them are now accepted as useful antioxidants [8], anticancer [9] and melanin synthesis regulating agents [10], superoxide anion-scavengers [11], anti-inflammatory agents [12], and compounds with antihypertensive [13], antinociceptive [14], antibiotic [15], and antiviral activity [16], *i.e.*, organoselenium compounds are nowadays an important class of biologically active products [17] with pharmaceutical applications [18].

The interest in Se compounds may also be attributed to their specific chemical properties, which fit well into the requirements of modern organic synthesis, and many of them are well adapted to chemo-, regio- and stereoselective reactions [19][20].

For all of these reasons, isoselenocyanates became a focus of interest in our research group as building blocks in the synthesis of Se-containing heterocycles. Their special chemical properties [21] make them very useful starting materials in heterocyclic chemistry [22], as they are easy to prepare and safe to store [23]. Nevertheless, under mild conditions, they undergo reactions, which are compatible with the presence of a variety of unsaturated as well as multi-functional structural units. Therefore, they are useful reagents in the preparation of natural products [24].

Within the family of triazoles, the corresponding thiones have gained especial importance. Several examples were described to be of pharmaceutical interest, *e.g.*, as agents with antibacterial activity [25]. A series of 1,2,4-triazolethiones have been prepared by using isothiocyanates [25–27] (and refs. cited therein). For example, 3,4-dihydro-2*H*-1,2,4-triazole-3-thione derivatives were synthesized by the reaction of isothiocyanates with amidrazone hydrochlorides [26]. Correspondingly, 5-amino derivatives were obtained when *S*-methyl isothiosemicarbazide hydroiodide (**1**) [28] was reacted with primary aryl- or benzylamines, and the resulting guanidinium iodide **2** was subsequently treated with aryl isothiocyanates in EtOH [25b] (*Scheme 1*). Depending on the reaction temperature, 5-arylamino- (**3**) or 5-amino-1,2,4-triazole-3-thiones (**4**) were isolated.

*Scheme 1*

As for the reaction of isoselenocyanates with nucleophiles, it is known that N, O, S, and Se-nucleophiles add to the central C-atom [21a], whereas P-nucleophiles attack either the central C-atom or the Se-atom [21b][29]. However, only a few examples have been reported for the reaction of hydrazine derivatives with isoselenocyanates [30] and nothing is known on the reaction with guanidine compounds. Very recently, we have published the synthesis of 1,3,4-selenadiazine derivatives from hydrazine,  $\alpha$ -bromoacetophenones and isoselenocyanates [31].

As a continuation of the previously published studies on the synthesis of Se-containing heterocycles based on isoselenocyanate chemistry [32], we have recently reported on the synthesis of 5-selenoxo-1,2,4-triazole-1-carboxylates by using a *Mitsunobu* strategy [33]. Following a similar strategy, *Koketsu et al.* have published the preparation of 3-selenoxo-1,2,4-triazole derivatives by the reaction of acyl isoselenocyanates with phenyl hydrazine [30]. Furthermore, reactions of isoselenocyanates **5** with mercapto acids led to 2-selenoxo-1,3-thiazolidin-4-ones and 2-selenoxo-1,3-thiazinan-4-ones in good yields [34].

In the present paper, the results of the investigations aimed at extending this methodology to the synthesis of 5-amino-1,2,4-triazole-3-selone derivatives are reported.

**2. Results and Discussion.** – In the synthesis of the 1,3,4-selenadiazine derivatives [31], hydrazine was used as a bisnucleophilic reagent, which combined first with the aryl isoselenocyanate **5** and, in a later reaction step, underwent the cyclization with the acetophenone residue of the intermediate. In this case, cyclization occurred *via* a condensation

reaction. We report here the use of *S*-methyl thiosemicarbazide (**1**) bearing a methylthio group, which will be the leaving group in the cyclization step of the preparation of 5-amino-4-aryl-2*H*-1,2,4-triazole-3-selones **7** according to *Scheme 2*. After stirring for 12 h, the products were separated by filtration; they were obtained in good yields and were pure enough to give unambiguous spectroscopic data and elemental analyses (*Table 1*).

### *Scheme 2*

### *Table 1*

The structures of compounds **7** were established on the basis of their spectroscopic data, which correspond reasonably well with those of the previously described 5-selenoxo-1,2,4-triazole-1-carboxylates [33]. In the IR-spectra (KBr), the triazoleselones **5** show weak absorptions for NH at 3380–3150 cm<sup>-1</sup> and a strong C=N absorption at *ca.* 1640 cm<sup>-1</sup>. The <sup>1</sup>H-NMR signals for the NH and NH<sub>2</sub> groups in CDCl<sub>3</sub> appear at 13.6–12.9 and 6.5–5.3 ppm, respectively. Characteristic signals in the <sup>13</sup>C-NMR spectra are observed for the triazole C-atoms (C(5) and C(3)) at 152–159 ppm. Furthermore, the ESI-MS show the [M+Na]<sup>+</sup> signal as the characteristic ensemble of the peaks for the Se isotopes.

A reaction mechanism for the formation of **7** is proposed in *Scheme 2*. After deprotonation of the hydroiodide **1**, nucleophilic addition of *S*-methyl isothiosemicarbazide onto **5** leads to an intermediate **6**, which undergoes a cyclization *via* elimination of MeSH.

Although all analytical data are in accordance with structure **7**, we cannot exclude the tautomeric structures **8** and **9** with certainty. Even structure **10**, which could be the result of the alternative cyclization of **6** *via* the Se-atom, is compatible with the data. Therefore, we decided to prove the structure by X-ray crystallography. However, the triazoles **7**, which were obtained directly from the reaction mixture after filtration, were always amorphous, and the crystallization of these products proved to be a difficult task. An explanation for this behavior could be the presence of NH groups with the possibility of the formation of different tautomeric structures (*i.e.* **7–9**). The recrystallization needed rather polar solvents, and the formation of metallic Se and decomposition of the product was observed even at low temperature. After several attempts, crystallization of **7a** from MeOH/CH<sub>2</sub>Cl<sub>2</sub> gave orange crystals with a m.p. 206–208° and a molecular weight of 478 (ESI-MS). Therefore, the structure of the recrystallized product was proposed to be the diselenide **11a**, which could be formed from the tautomeric triazoleselenol **9a** by oxidative dimerization (*Scheme 3*). This assumption was proven by an X-ray crystal-structure determination (*Fig. 1*).

### *Scheme 2*

Figure 1. *ORTEP Plot* [35] *of the molecular structure of 11a* (arbitrary numbering of atoms; 50% probability ellipsoids)

The asymmetric unit in the crystal structure contains one molecule of **11a**, one MeOH molecule and two molecules of H<sub>2</sub>O (*Fig. 2*). The five-membered heterocyclic rings are planar, with the adjacent atoms N(3), Se(1) and N(14), C(17), respectively, also being in the corresponding plane, while C(6) and Se(2) deviate by 0.213(2) and 0.114(1) Å, respectively,



from these planes. The torsion angle C(1)–Se(1)–Se(2)–C(12) is  $-96.08(9)^\circ$ , as usually observed for oligosulfanes and di- and triselenides (see, *e.g.*, [36][37]). The planes of the Ph groups at N(2) and N(13) are significantly twisted out of the planes of their parent heterocyclic rings with the dihedral angles between the planes being  $87.95(11)$  and  $55.67(11)^\circ$ , respectively.

Figure 2. *The molecular packing of 11a projected down the a-axis showing the H-bonding scheme (equivalent isotropic spheres for atoms; uninvolved H-atoms omitted for clarity)*

Intermolecular H-bonds link the molecules of **11a**, MeOH and H<sub>2</sub>O into a three-dimensional framework. Each molecule of **11a** donates H-bonds to one neighboring molecule of **11**, as well as to three different H<sub>2</sub>O molecules. One of the two symmetry-independent H<sub>2</sub>O molecules donates H-bonds to two different molecules of **11a**. The other H<sub>2</sub>O molecule donates one H-bond to a molecule of **11a** and a second H-bond to the O-atom of a MeOH molecule. The MeOH molecule donates a H-bond to one of the H<sub>2</sub>O molecules. The H-bond acceptor atoms in **11a** are the unsubstituted N-atoms in the five-membered rings.

In conclusion, we have shown that isoselenocyanates **5** react with isothiosemicarbazide hydroiodide **1** in basic media to give an intermediate, which undergoes a ring formation to give 4-aryl-3,4-dihydro-2*H*-1,2,4-triazole-5-selones **7** in good yields. These products are easily oxidized to give bis(triazol-3-yl)diselenides **11**.

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## Experimental Part

1. *General*. See [32e][32f]. TLC: silica gel 60  $F_{254}$  plates (0.25 mm; *Merck*). Column chromatography (CC): silica gel 60 (0.040-0.063 mesh; *Merck*). M.p.: *Büchi B-540* apparatus in capillaries; uncorrected.  $^1\text{H}$ -NMR (300 MHz) and  $^{13}\text{C}$ -NMR (75.5 MHz) spectra: *Bruker ARX-300* instrument, in  $(\text{D}_6)\text{DMSO}$  unless otherwise specified; chemical shifts in ppm. ESI-MS: *Finnigan MAT TSQ-700* instrument.

2. *Starting Materials*. Isoselenocyanates were prepared according to *Barton's* procedure starting from formamides [23]. Formanilide is commercially available (*Fluka*), *N*-(4-bromophenyl)-, *N*-(4-chlorophenyl)-, *N*-(4-methylphenyl)-, and *N*-(4-methoxyphenyl)-formamide were prepared from the respective commercial anilines and 95%  $\text{HCOOH}$  [38]. The soln. was heated to reflux for 30 min and evaporated to dryness *in vacuo*. The residue was dissolved in  $\text{Et}_2\text{O}$  and washed with diluted  $\text{AcOH}$  (5%),  $\text{H}_2\text{O}$  and aq.  $\text{NaHCO}_3$  (5%). The aq. phase was extracted with  $\text{Et}_2\text{O}$ , the combined org. extracts were dried ( $\text{MgSO}_4$ ) and evaporated *i.v.* The crude products were purified by recrystallization in  $\text{H}_2\text{O}$ . *S*-Methylisothiosemicarbazide hydroiodide (**1**) was prepared by treatment of thiosemicarbazide

(9.10 g, 0.10 mol) with MeI (14.20 g, 0.10 mol) in refluxing abs. EtOH for 2 h. The mixture was allowed to cool, and filtration and purification by recrystallization in abs. EtOH yielded 18.71 g (80%) of **1**. M.p. = 137–139° ([39]: 138°). <sup>1</sup>H-NMR: 2.69 (*s*, Me). <sup>13</sup>C-NMR: 12.7 (Me); 170.2 (C). ESI-MS: 234 (2, [M+1]<sup>+</sup>), 106 (100, C<sub>2</sub>H<sub>8</sub>N<sub>3</sub>S<sup>+</sup>), 92 (53). Anal. calc. for C<sub>2</sub>H<sub>8</sub>N<sub>3</sub>SI (233.07): C 10.31, H 3.46, N 18.03, S 13.76; found: C 10.30, H 3.44, N 18.24, S 13.59.

*3. General Procedure for the Preparation of 1,2,4-Triazole-3-selones 7.* A 25 ml round-bottom flask equipped with a magnetic stirrer and a condenser was charged with a soln. of **1** (233 mg, 1.0 mmol) and the respective isoselenocyanate **5** (1.0 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (20 ml). Then, Et<sub>3</sub>N (0.28 ml, 2.0 mmol) was added, whereby the suspension became instantaneously colorless and then rapidly yellow. The evolution of a gas (methanethiol) was detected. The mixture was stirred overnight, then, the white precipitate was filtered and washed with cold CH<sub>2</sub>Cl<sub>2</sub> to give analytically pure product.

*5-Amino-3,4-dihydro-4-phenyl-2H-1,2,4-triazole-3-selone (7a).* From phenylisoselenocyanate (**5a**). Yield: 187 mg (78%). White crystals. M.p. 191–193° (CH<sub>2</sub>Cl<sub>2</sub>). IR (KBr): 3363*w*, 3287*w*, 3249*w*, 3158*m* (br), 2970*w*, 2936*w*, 2785*w*, 1640*s*, 1593*m*, 1496*s*, 1450*m*, 1336*m*, 1237*m*, 1139*w*, 1071*w*, 1011*w*, 991*w*, 784*w*, 749*m*, 690*s*, 567*m*. <sup>1</sup>H-NMR: 5.94 (*br. s*, NH<sub>2</sub>); 7.25 (*d*, *J* = 8.1, 2 arom. H); 7.42–7.49 (*m*, 3 arom. H); 13.57 (*br. s*, NH). <sup>13</sup>C-NMR: 128.4 (2 arom. CH); 129.2 (3 arom. CH); 133.3 (1 arom. C); 153.1 (C(5)); 155.8 (C=Se). ESI-MS: 265 (12), 264 (10), 263 (100, [M+Na]<sup>+</sup>), 262 (5), 261 (47), 260 (14), 259 (13). Anal. calc. for C<sub>8</sub>H<sub>8</sub>N<sub>4</sub>Se (239.14): C 40.18, H 3.37, N 23.43; found: C 39.93, H 3.49, N 23.20.

*5-Amino-3,4-dihydro-4-(4-methoxyphenyl)-2H-1,2,4-triazole-3-selone (7b)*. From (4-methoxyphenyl)isoselenocyanate (**5b**). Yield: 194 mg (72%). White crystals. M.p. 177–179° (CH<sub>2</sub>Cl<sub>2</sub>). IR (KBr): 3373<sub>w</sub>, 3307<sub>w</sub>, 3261<sub>w</sub>, 3200<sub>w</sub>, 3158<sub>w</sub>, 2999<sub>w</sub>, 2935<sub>w</sub>, 2808<sub>w</sub>, 1646<sub>s</sub>, 1604<sub>w</sub>, 1583<sub>w</sub>, 1513<sub>s</sub>, 1459<sub>m</sub>, 1442<sub>m</sub>, 1338<sub>m</sub>, 1302<sub>m</sub>, 1259<sub>s</sub>, 1240<sub>m</sub>, 1184<sub>w</sub>, 1170<sub>m</sub>, 1130<sub>m</sub>, 1103<sub>w</sub>, 1048<sub>w</sub>, 1021<sub>w</sub>, 1007<sub>w</sub>, 989<sub>w</sub>, 833<sub>m</sub>, 803<sub>w</sub>, 768<sub>w</sub>, 728<sub>w</sub>, 665<sub>w</sub>, 629<sub>w</sub>, 619<sub>w</sub>, 573<sub>w</sub>. <sup>1</sup>H-NMR: 4.06 (*s*, MeO); 6.25 (*br. s*, NH<sub>2</sub>); 7.31, 7.49 (AA'BB', *J* = 8.1, 4 arom. H); 13.52 (*br. s*, NH). <sup>13</sup>C-NMR: 55.3 (MeO); 114.4 (2 arom. CH); 125.8 (1 arom. C); 129.7 (2 arom. CH); 153.3 (1 arom. C); 156.1 (C(5)); 159.5 (C=Se). ESI-MS: 295 (12), 294 (11), 293 (100, [M+Na]<sup>+</sup>), 292 (9), 291 (45), 290 (16), 289 (18). Anal. calc. for C<sub>9</sub>H<sub>10</sub>N<sub>4</sub>OSe (269.17): C 40.16, H 3.74, N 20.82; found: C 40.31, H 3.40, N 21.06.

*5-Amino-3,4-dihydro-4-(4-methylphenyl)-2H-1,2,4-triazole-3-selone (7c)*. From (4-methylphenyl)isoselenocyanate (**5c**). Yield: 203 mg (80%). White crystals. M.p. 182–184° (CH<sub>2</sub>Cl<sub>2</sub>). IR (KBr): 3367<sub>w</sub>, 3298<sub>w</sub>, 3255<sub>w</sub>, 3159<sub>w</sub>, 2999<sub>w</sub>, 2942<sub>w</sub>, 2798<sub>w</sub>, 1645<sub>s</sub>, 1599<sub>w</sub>, 1578<sub>w</sub>, 1500<sub>s</sub>, 1465<sub>m</sub>, 1443<sub>m</sub>, 1332<sub>m</sub>, 1295<sub>m</sub>, 1245<sub>m</sub>, 1240<sub>m</sub>, 1178<sub>w</sub>, 1165<sub>m</sub>, 1128<sub>m</sub>, 1105<sub>w</sub>, 1055<sub>w</sub>, 1018<sub>w</sub>, 1000<sub>w</sub>, 978<sub>w</sub>, 835<sub>w</sub>, 798<sub>w</sub>, 777<sub>w</sub>, 725<sub>w</sub>, 656<sub>w</sub>. <sup>1</sup>H-NMR: 2.42 (*s*, Me); 5.28 (*br. s*, NH<sub>2</sub>); 7.26, 7.30 (AA'BB', *J* = 8.1, 4 arom. H); 12.91 (*br. s*, NH). <sup>13</sup>C-NMR: 20.6 (Me); 127.1 (2 arom. CH); 129.7 (1 arom. C); 129.8 (2 arom. CH); 139.3 (1 arom. C); 156.1 (C(5), C=Se). ESI-MS: 279 (12), 278 (12), 277 (100, [M+Na]<sup>+</sup>), 276 (7), 275 (55), 274 (12), 273 (17). Anal. calc. for C<sub>9</sub>H<sub>10</sub>N<sub>4</sub>Se (253.17): C 42.70, H 3.98, N 22.13; found: C 42.56, H 4.12, N 22.23.

*5-Amino-4-(4-bromophenyl)-3,4-dihydro-2H-1,2,4-triazole-3-selone (7d)*. From (4-bromophenyl)isoselenocyanate (**5d**). Yield: 261 mg (82%). White crystals. M.p. 192–194°

(CH<sub>2</sub>Cl<sub>2</sub>). IR (KBr): 3383<sub>w</sub>, 3294<sub>w</sub>, 3080<sub>m</sub> (br), 2927<sub>w</sub>, 2774<sub>w</sub>, 1633<sub>s</sub>, 1586<sub>m</sub>, 1573<sub>m</sub>, 1489<sub>m</sub>, 1450<sub>m</sub>, 1403<sub>w</sub>, 1330<sub>m</sub>, 1226<sub>m</sub>, 1103<sub>w</sub>, 1069<sub>w</sub>, 1005<sub>m</sub>, 985<sub>w</sub>, 835<sub>m</sub>, 820<sub>w</sub>, 771<sub>w</sub>, 741<sub>w</sub>, 715<sub>w</sub>, 570<sub>m</sub>. <sup>1</sup>H-NMR: 6.46 (*br. s*, NH<sub>2</sub>); 7.63, 8.05 (AA'BB', *J* = 8.1, 4 arom. H); 13.42 (*br. s*, NH). <sup>13</sup>C-NMR: 122.5 (1 arom. C); 130.8 (2 arom. CH); 132.2 (2 arom. CH); 139.4 (1 arom. C); 152.9 (C(5)); 155.8 (C=Se). ESI-MS: 345 (13), 344 (8), 343 (78), 342 (11), 341 (100, [M+Na]<sup>+</sup>), 340 (16), 339 (48), 338 (15), 337 (12). Anal. calc. for C<sub>8</sub>H<sub>7</sub>BrN<sub>4</sub>Se (318.04): C 30.21, H 2.22, N 17.62; found: C 30.36, H 2.55, N 17.63.

*5-Amino-4-(4-chlorophenyl)-3,4-dihydro-2H-1,2,4-triazole-3-selone* (**7e**). From (4-chlorophenyl)isoselenocyanate (**5e**). Yield: 205 mg (75%). White crystals. M.p. 185–187° (CH<sub>2</sub>Cl<sub>2</sub>). IR (KBr): 3379<sub>w</sub>, 3294<sub>w</sub>, 3084<sub>m</sub> (br), 2958<sub>m</sub>, 2931<sub>m</sub>, 2778<sub>w</sub>, 1634<sub>s</sub>, 1587<sub>m</sub>, 1574<sub>m</sub>, 1493<sub>s</sub>, 1453<sub>m</sub>, 1409<sub>w</sub>, 1331<sub>m</sub>, 1230<sub>m</sub>, 1106<sub>w</sub>, 1091<sub>w</sub>, 1007<sub>m</sub>, 986<sub>w</sub>, 840<sub>m</sub>, 822<sub>w</sub>, 774<sub>w</sub>, 734<sub>w</sub>, 717<sub>w</sub>, 574<sub>m</sub>. <sup>1</sup>H-NMR: 6.33 (*br. s*, NH<sub>2</sub>); 7.58, 7.79 (AA'BB', *J* = 8.7, 4 arom. H); 13.47 (*br. s*, NH). <sup>13</sup>C-NMR: 129.3 (2 arom. CH); 130.5 (2 arom. CH); 132.2 (1 arom. C); 133.9 (1 arom. C); 153.0 (C(5)); 155.8 (C=Se). CI-MS (NH<sub>3</sub>): 277 (3), 275 (7, [M+1]<sup>+</sup>), 273 (4), 197 (34), 196 (12), 195 (100), 194 (6). Anal. calc. for C<sub>8</sub>H<sub>7</sub>ClN<sub>4</sub>Se (273.59): C 35.12, H 2.58, N 20.48; found: C 34.90, H 2.80, N 20.34.

*Bis(5-amino-4-phenyl-1,2,4-triazol-3-yl)diselenide* (**11a**). Repeated attempts to crystallize **7a** from CH<sub>2</sub>Cl<sub>2</sub> gave orange crystals of **11a**. M.p. 206.0–208.3° (color change). <sup>1</sup>H-NMR: 6.05 (*br. s*, 2 NH<sub>2</sub>); 6.97 (*d*-like, 4 arom. H); 7.42–7.50 (*m*, 6 arom. H). ESI-MS: 504 (9), 503 (29), 502 (20), 501 (100, [M+Na]<sup>+</sup>), 500 (21), 499 (77), 498 (31), 497 (43), 496 (13), 495 (17), 479 (19, [M+1]<sup>+</sup>), 477 (17).

*X-Ray Crystal-Structure Determination of 11a* (see Fig. 1 and Table 2)<sup>3</sup>). All measurements were made on a *Nonius KappaCCD* diffractometer [40] using graphite-monochromated  $\text{MoK}\alpha$  radiation ( $\lambda$  0.71073 Å) and an *Oxford Cryosystems Cryostream 700* cooler. Data reduction was performed with *HKL Denzo* and *Scalepack* [41]. The intensities were corrected for *Lorentz* and polarization effects, and an absorption correction based on the multi-scan method [42] was applied. Equivalent reflections were merged. Data collection and refinement parameters are given in Table 2, and a view of the molecule is shown in the Figure. The structure was solved by direct methods using *SHELXS97*[43], which revealed the positions of all non-H-atoms. The asymmetric unit contains one molecule of the Se-compound, one MeOH molecule and two molecules of H<sub>2</sub>O. The non-H-atoms were refined anisotropically. The NH<sub>2</sub>, H<sub>2</sub>O and hydroxy H-atoms were placed in the positions indicated by a difference electron density map and their positions were allowed to refine together with individual isotropic displacement parameters. All remaining H-atoms were placed in geometrically calculated positions and refined using a riding model where each H-atom was assigned a fixed isotropic displacement parameter with a value equal to 1.2U<sub>eq</sub> of its parent C-atom (1.5 U<sub>eq</sub> for the Me group of the MeOH molecule). Refinement of the structure was carried out on  $F^2$  using full-matrix least-squares procedures, which minimized the function  $\sum w(F_o^2 - F_c^2)^2$ . A correction for secondary extinction was applied. Four reflections, whose intensities were considered to be extreme outliers, were omitted from the final refinement. Neutral atom scattering factors for non-H-atoms were taken from [44], and the scattering factors for H-atoms were taken from [45]. Anomalous dispersion effects were included in  $F_c$

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<sup>3</sup>) CCDC-631597 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the *Cambridge Crystallographic Data Centre* via [www.ccdc.cam.ac.uk/data-request/cif](http://www.ccdc.cam.ac.uk/data-request/cif).

[46]; the values for  $f'$  and  $f''$  were those of [47]. The values of the mass attenuation coefficients are those of [48]. All calculations were performed using the SHELXL97 [49] program.

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*Captions*

Table 1. *Preparation of 5-Amino-3,4-dihydro-2H-1,2,4-triazole-5-selones **7** from Isoselenocyanates **5***

Table 2. *Crystallographic Data of Compound **11a***

Figure 2: *The molecular packing of **11a** projected down the a-axis showing the H-bonding scheme (equivalent isotropic spheres for atoms; uninvolved H-atoms omitted for clarity)*

Table 1: *Preparation of 5-Amino-3,4-dihydro-2H-1,2,4-triazole-5-selones **7** from Isoselenocyanates **5***

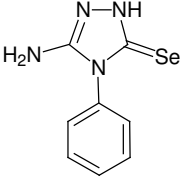
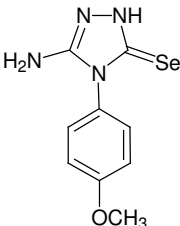
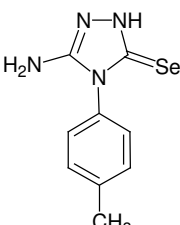
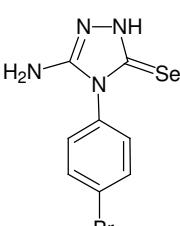
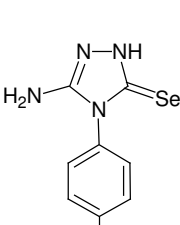
| Entry    | R <sup>1</sup>                      | <b>7</b>  | Yield (%) |
|----------|-------------------------------------|---|-----------|
| <b>a</b> | Ph                                  |    | 78        |
| <b>b</b> | 4-MeO-C <sub>6</sub> H <sub>4</sub> |    | 72        |
| <b>c</b> | 4-Me-C <sub>6</sub> H <sub>4</sub>  |   | 80        |
| <b>d</b> | 4-Br-C <sub>6</sub> H <sub>4</sub>  |  | 82        |
| <b>e</b> | 4-Cl-C <sub>6</sub> H <sub>4</sub>  |  | 75        |

Table 2. *Crystallographic Data of Compound 11a*

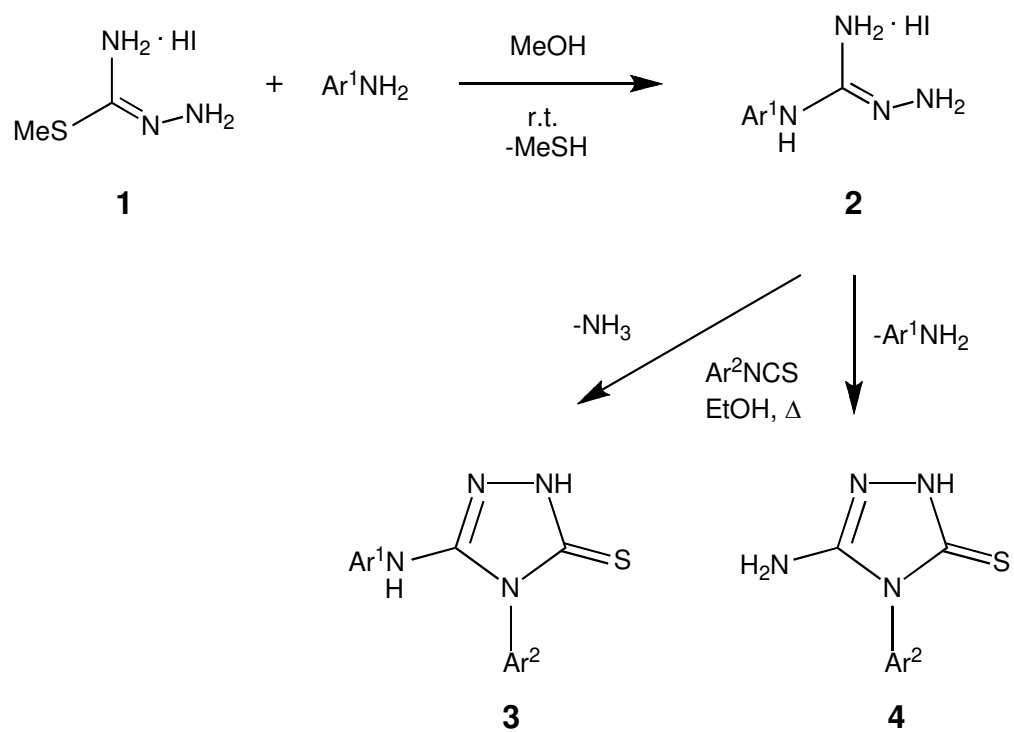
|  |   |
|--|---|
| Crystallized from                            | CH <sub>2</sub> Cl <sub>2</sub> /MeOH   |
| Empirical formula                            | C <sub>17</sub> H <sub>22</sub> N <sub>8</sub> O <sub>3</sub> Se <sub>2</sub>       |
| Formula weight [g mol <sup>-1</sup> ]        | 544.33  |
| Crystal color, habit                         | orange, tablet  |
| Crystal dimensions [mm]                      | 0.10 × 0.22 × 0.28  |
| Temperature [K]                              | 160(1)  |
| Crystal system                               | monoclinic  |
| Space group                                  | <i>P</i> 2 <sub>1</sub> / <i>n</i>  |
| <i>Z</i>                                     | 4   |
| Reflections for cell determination           | 65007   |
| 2 $\theta$ range for cell determination [°]  | 4–60  |
| Unit cell parameters                         |   |
| <i>a</i> [Å]                                 | 8.6743(1)   |
| <i>b</i> [Å]                                 | 14.3351(1)  |
| <i>c</i> [Å]                                 | 17.8878(2)  |
| $\beta$ [°]                                  | 102.8824(6)   |
| <i>V</i> [Å <sup>3</sup> ]                   | 2168.31(4)  |
| <i>D<sub>x</sub></i> [g cm <sup>-3</sup> ]   | 1.667   |
| $\mu$ (MoK $\alpha$ ) [mm <sup>-1</sup> ]    | 3.447   |
| Scan type                                    | $\phi$ and $\omega$   |
| 2 $\theta_{\text{(max)}}$ [°]                | 60  |
| Transmission factors (min; max)              | 0.492; 0.717  |
| Total reflections measured                   | 55961   |
| Symmetry independent reflections             | 6352  |
| Reflections with $I > 2\sigma(I)$            | 5010  |
| Reflections used in refinement               | 6348  |
| Parameters refined                           | 309   |
| Final $R(F)$ [ $I > 2\sigma(I)$ reflections] | 0.0340  |
| $wR(F^2)$ (all data)                         | 0.0841  |
| Weights:                                     | $w = [\sigma^2(F_o^2) + (0.0433P)^2 + 0.7378P]^{-1}$ where $P = (F_o^2 + 2F_c^2)/3$ |

|  |             |
|--|-------------|
| Goodness of fit                              | 1.034       |
| Secondary extinction coefficient             | 0.0010(3)   |
| Final $\Delta_{\max}/\sigma$                 | 0.001       |
| $\Delta\rho$ (max; min) [e Å <sup>-3</sup> ] | 0.62; -0.91 |

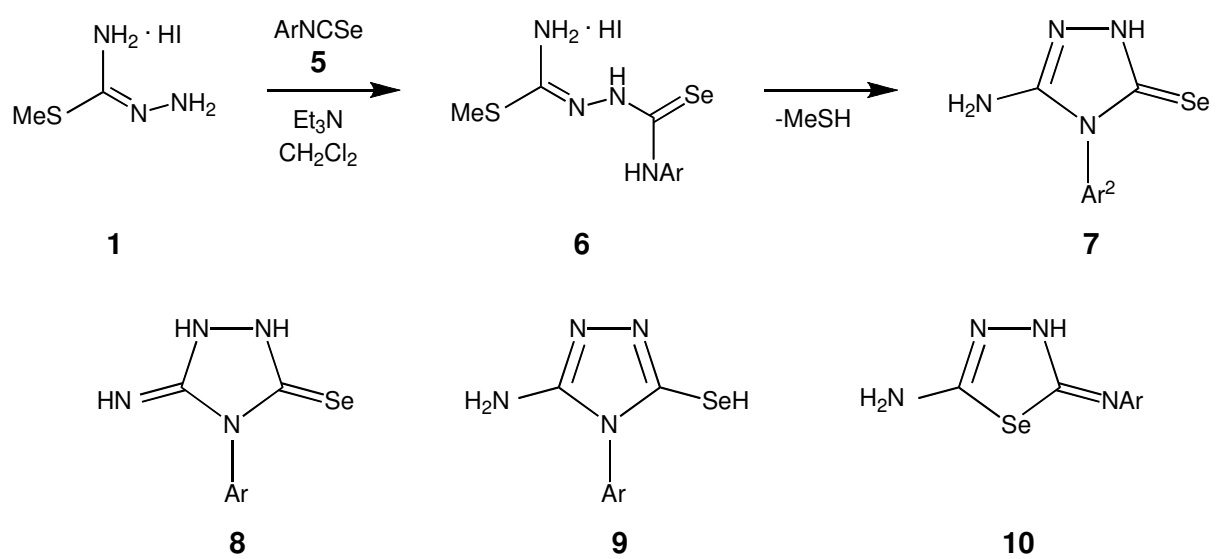
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Scheme 1



## Scheme 2



Scheme 3

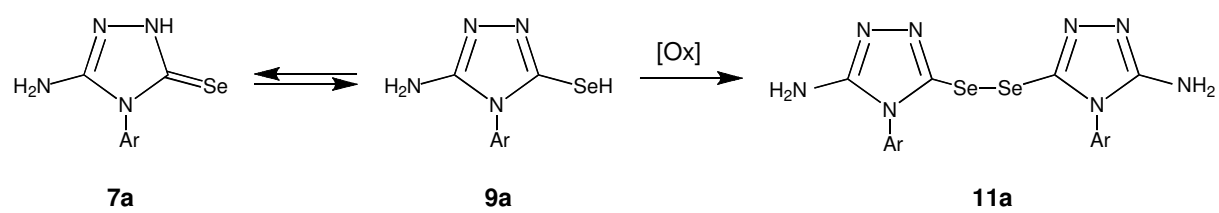


Figure 1. ORTEP Plot [48] of the molecular structure of **11a** (arbitrary numbering of atoms; 50% probability ellipsoids)

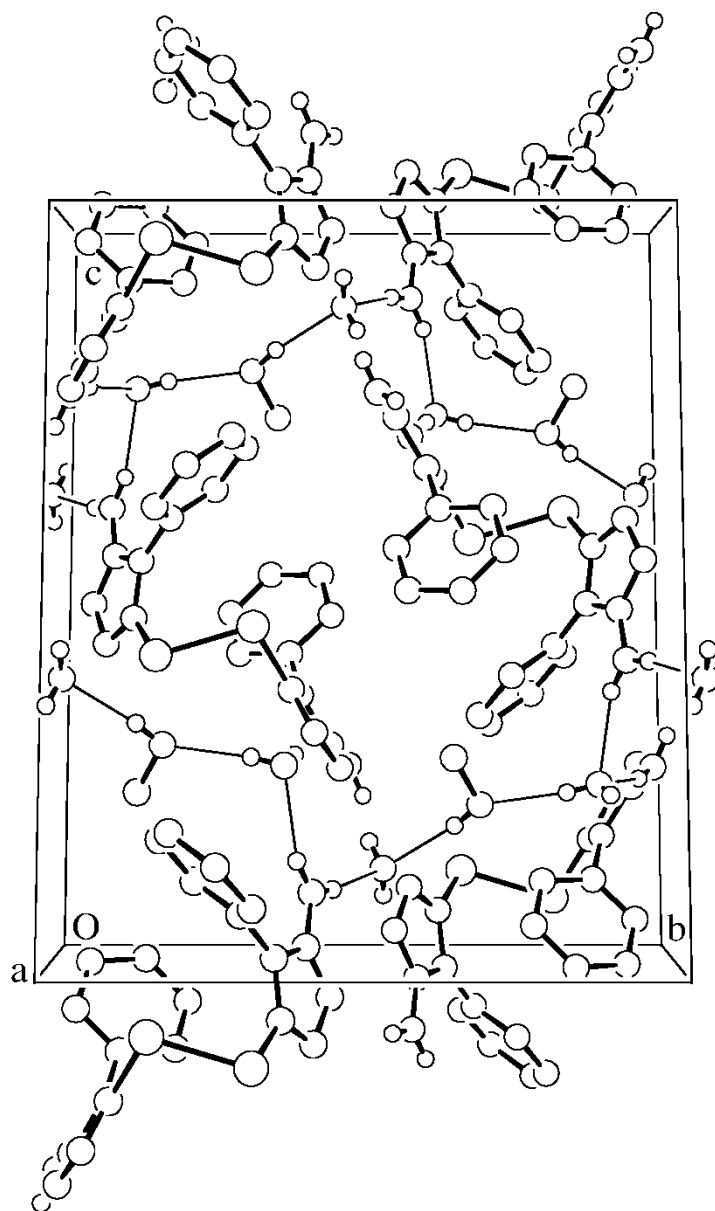


Figure 2: *The molecular packing of **11a** projected down the a-axis showing the H-bonding scheme (equivalent isotropic spheres for atoms; uninvolved H-atoms omitted for clarity)*

*Graphical Abstract*